

Remarks

Claims 47-58 are pending. Claims 47 and 48 are amended and Claim 50 is cancelled without prejudice or disclaimer.

The specification is objected to for translation errors, for example, regarding the term “planktonic.” The Applicants submit that paragraph [0007] of the specification has been amended to correct the error noted in the Official Action. The Applicants respectfully submit that the objection is moot.

The title is objected to because it is not descriptive of the claimed subject matter. The Applicants respectfully submit that the title, as amended, recites a “Method and device for detecting the formation and development of microorganism biofilms in a liquid culture medium.” The Applicants submit that the amended title adequately describes the subject matter to which the claims are directed. Reconsideration and withdrawal of the objection to the title are respectfully requested.

The Abstract is objected to for being in improper format. The Applicants respectfully submit that the Abstract was amended by Preliminary Amendment on June 26, 2007 and is in compliance with 37 CFR §1.72. The Applicants invite the Examiner’s attention to page 29 of the Preliminary Amendment which contains previous amendments to the Abstract. Reconsideration and withdrawal of the objection to the Abstract are respectfully requested.

Claims 47-58 are rejected under 35 USC §103(a) as being unpatentable over Surette in view of Cronin-Golumb. The rejection states that Surette discloses placing magnetic beads in a culture medium that may be manipulated by a magnetic field and the formation of a biofilm on the beads. The Official Action concedes that Surette fails to teach or suggest that a change in the motion of a bead is indicative of a change in viscosity and formation of a biofilm. The rejection relies on Cronin-Golumb for teaching that magnetic beads are oscillated by a varying magnetic field to give information on viscosity.

The Applicants respectfully submit that Claims 47-58 are not obvious in view of the combination of Surette and Cronin-Golumb and that they cannot be combined to obtain the subject matter of Claims 47-58. Surette describes a purification process, very similar to other purification of molecules (DNA, proteins) or cells (prokaryotes, fungi, eucaryotes...) on magnetic microbeads : 1) selective interaction of molecules or cells on beads, 2) removal of magnetic beads from the liquid medium by a magnet, 3) washing of these beads, 4) desorption of

adherents molecules or cells from beads. In sharp contrast, the Applicants' claimed subject matter is based on: no bead isolation and no washing. The key of the Applicants' concept is the use of the magnetic beads to test *in situ*, with only the magnetic field strength at distance, in the liquid medium, the presence of a biofilm without any invasive action (washing, staining...). Surette pertains to isolating a microorganism by a process that requires removal of the beads from the medium to determine if the microorganism biofilm has adhered to the bead. See Surette at page 6, lines 13-29 and the Examples. A magnet is used to remove a bead from the medium by either allowing the bead to adhere to the magnet and removing the magnet with bead from the medium or using the magnet to adhere the bead to the wall of the receptacle and removing the medium from the receptacle. This is the only purpose of the magnet in Surette in the way of a purification process. By this way, Surette could detect an isolated adherent cell, but an isolated adherent cell is not a biofilm. A biofilm is a mat of cells, with more than one bacterium, and often these bacteria secrete a viscous matrix (usually named slime). The presence of this viscous matrix is detected by the Applicants' concept and not by Surette. As acknowledged in the rejection, at no point does Surette teach or suggest a method comprising using a magnet in the step of quantifying or detecting the formation of a biofilm. This is because Surette's method requires washing of the beads to determine if the biofilm formed on the bead. For example, Surette teaches that the bead is sonicated or washed with SDS to remove the cells comprising the biofilm from the bead surface and the biofilm is detected by plating the cells.

Surette neither teaches nor suggests that the biofilm can be detected while the biofilm is still adhered to the bead, while the bead is still in the medium, or while the bead is interacting with the magnet. Surette provides disclosure only relevant to the detection of the individual adhered cells and not the viscous matrix. This is significant for two reasons. First, because Surette teaches that the bead is removed from the medium to detect the biofilm, it does not teach or suggest a method of detecting the formation of a biofilm "in a liquid medium" as specified in Claim 47. Second, because Surette pertains to detection of a biofilm after washing of the beads, which eliminates the bacteria that are not really adherent (by elements of the cell body like filaments, pili, fimbriae, curli...), but only "sticked" by the viscous matrix, one skilled in the art in view of Surette would be guided away from modifying Surette to enable direct detection of the biofilm on the bead. Accordingly, one skilled in the art would be guided away from the modification of Surette's method that is contemplated by the rejection.

In any event, the Applicants respectfully submit that one skilled in the art would not look to the combination of Surette with Cronin-Golumb for a method of detecting the formation of a biofilm on a bead because Cronin-Golumb teaches a process that prohibits the formation of the biofilm. Cronin-Golumb discloses a method for determining the local viscoelasticity of a medium using a scanning optical microscope to observe a particle in constant motion. The phase delay of the second harmonic is used to calculate the viscosity. While particle motion is critical to Cronin-Golumb's invention, it also precludes the formation of a biofilm on the particle. Accordingly, the combination of Cronin-Golumb with Surette would frustrate Surette's objective of detecting biofilm formation on a bead.

Moreover, even if the combination were possible, the result is distinct from the method recited in Claims 47-58 because it would not permit direct detection of the formation of a biofilm in a liquid medium. Neither reference teaches or suggests a method that allows direct determination of the formation of a biofilm. Accordingly, the combination does not teach the method recited in Claims 47-58.

Additionally, Cronin-Golumb's methods are also very complicated and require sophisticated devices and complex steps that make reproduction of the results difficult. In contrast, the methods recited in Claims 47-58 allow the detection of the formation of a biofilm without complicated equipment or an extensive process. Thus, one skilled in the art would not have been motivated to look to Cronin-Golumb or arrived at the subject matter of Claims 47-58.

Furthermore, the Applicants submit that rejections for obviousness cannot be sustained by mere conclusory statements. Instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. Here, the rejection fails to articulate a particular motivation for combining the references or modifying Surette. It only makes a blanket statement that it would have been obvious to detect the change in viscosity with the formation of a biofilm because it would have been known that the biofilm would change the motion of the particles. The Applicants respectfully submit that it appears that the only explanation for the rejection is that it is relying on hindsight and using the Applicants' specification as a blueprint. This is an improper basis for a rejection under §103.

In view of the foregoing, the Applicants respectfully submit that Claims 47-58 are not obvious in view of Surette and Cronin-Golumb. Reconsideration and withdrawal of the rejection under 35 USC §103 are respectfully requested.

Claims 47-58 are rejected under 35 USC §112, first paragraph, for lack of enablement. The rejection states that the specification supports detecting a biofilm by moving a magnetic bead with a magnetic field, but it does not support detection methods including electrically charged particles or fluorescent, phosphorescent, radioactive, and chemiluminescent particles.

The purpose of the enablement requirement is to ensure that the specification describes the invention in such terms that one skilled in the art can make and use the claimed invention. Detailed procedures for making and using the invention are not necessary if the description of the invention itself is sufficient to permit those skilled in the art to make and use the invention without undue experimentation.

The Applicants respectfully submit that one skilled in the art at the time of filing in view of the specification would be able to make and use electrically charged particles for detecting the formation of a biofilm on the particle. One skilled in the art would appreciate that the application of electrical current to the liquid medium would cause positively or negatively charged particles to move. Moreover, the behavior of charged particles exposed to an electric field is neither unpredictable nor beyond the grasp of one skilled in the art at the time of filing. Accordingly, one skilled in the art could have readily made an electrically charged particle and would have understood how to apply an electric current to the medium and detect the motion of the charged particle based on the Applicants' specification and ordinary knowledge. Thus, the Applicants respectfully submit that this feature is enabled.

With respect to the detection of a biofilm using fluorescent, phosphorescent, radioactive, and chemiluminescent particles, the Applicants submit that one skilled in the art in view of the specification is readily able to make and use particles having those characteristics and, thus these features are enabled. The Applicants invite the Examiner's attention to paragraphs [0043], [0044], [0060] and [0062] of the specification which discuss the use of fluorescent, phosphorescent, radioactive and chemiluminescent particles. Such particles generate a detectable "signal" that can be used to observe and detect the motion of the particles. One skilled in the art at the time of filing had ample knowledge as to how to make particles that are fluorescent, phosphorescent, radioactive, or chemiluminescent and magnetic, electromagnetic, or electric. Similarly, one skilled in the art would understand how to detect the motion of such particles in a liquid medium. Undue experimentation is not required.

Accordingly, the Applicants respectfully submit that the rejected claims are fully enabled with respect to electrically charged, fluorescent, phosphorescent, radioactive and chemiluminescent particles. Reconsideration and withdrawal of the rejection under 35 USC §112 are respectfully requested.

Claims 47-58 are rejected under 35 USC §112, second paragraph, for indefiniteness. Specifically, the rejection states that there is a typo in Claim 47 and that the features of Claim 48 must be positively recited. Additionally, the rejection states that the terms “augmentation” and “motion field” in Claims 49 and 50 are unclear.

The Applicants respectfully submit that Claims 47 and 48 have been amended and Claim 50 has been cancelled. In light of the amendments to the claims, the Applicants respectfully submit that the rejection under 35 USC §112, second paragraph, is moot.

The Applicants respectfully submit that the specification defines the term “progressive augmentation” in Claim 49 at paragraph [0044] of the specification. Specifically, the progressive augmentation of the electromagnetic field may be obtained by approaching a magnet along a rectilinear or sinusoidal trajectory or even according to an oscillatory motion that can have or not have a variable oscillation amplitude and a variable frequency. More complex variations of the electromagnetic field may be obtained by rotation or by combinations of movements of a magnetized bar in the proximity of the culture. Accordingly, the Applicants respectfully submit that Claim 44 is definite and adequately describes the subject matter to which it pertains. Reconsideration and withdrawal of the rejection of Claim 49 are respectfully requested.

In light of the foregoing, the Applicants respectfully submit that the entire application is now in condition for allowance, which is respectfully requested.

Respectfully submitted,


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